INTERNET-SCALE CHEMICAL SENSING: IS IT MORE THAN A VISION?*

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Abstract In order to realise scalability of chemical sensors in extensively deployed wireless sensor networks, considerable materials challenges must be overcome. Conventional devices are currently far too expensive and unreliable for massive long-term field deployment. Cost can be driven down by imaginative approaches to transduction and instrument design. For example, we have produced a complete instrument based on LED measurement of colour changes that has sub-micromolar detection limits for a number of heavy metals for around $1.2 In its current form, the device also has a short distance wireless communications functionality and very low power consumption. However, chemical sensors capable of long-term reliability will require imaginative solutions to the key issue — how can the sensing films/membranes in chemical sensors maintain predictable characteristics in long term deployment?

The vision of 'internet-scale sensing' will only be realised through advances in materials science and a complete rethink of how we do chemical sensing. For example, fully autonomous sensing platforms must be completely self-reliant in terms of power, communications, reagents and consumables. The sensor network must be self-sustaining, meaning that as individual nodes become unreliable, new nodes are established, for example through physical replacement or through devices capable of self-repair/regeneration. In this chapter, these issues are presented, along with some recent advances mentioned above.

Keywords:

chemical sensors; biosensors; CWA; BWA; sensor nets; wireless; adhoc networks.

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1. Introduction

Digital communications networks are at the heart of modern society. The digitisation of communications in general, the development of the internet, and the availability of relatively inexpensive but powerful mobile computing technologies have together established a global communications network capable of instantly linking billions of people, places and objects. Complex documents can be instantly transmitted to multiple remote locations, and web sites provide a platform for real-time notification, archiving, dissemination and exchange of information on a global basis. This technology, in its many guises, is rapidly becoming completely pervasive, and the average person now has multiple associations with this digital world on a daily basis. However, this is only the foundation for the next wave of development — one that will provide a seamless interface between the 'molecular' and 'digital' worlds. The crucial missing part is the gateway through which these worlds will communicate — how can the digital world look into the molecular world and become truly self-aware?

We are currently in the midst of a global technological revolution driven by the internet and the 'WEB'. Incredible advances in digital video and audio technologies, coupled with equally astonishing breakthroughs in digital communications and computer power, have changed our lives in a profound manner, affecting almost every aspect of modern society. But what lies ahead? How will science and technology converge to catalyse the next stage in societal change? Paul Saffo, interviewed by Michio Kaku, states that 'In the 21st Century, the next revolution will be driven by cheap sensors linked to microprocessors and lasers' [1].

The move from traditional analogue land-line to digital mobile phones has been an important part of this communications revolution. Inexpensive GSM and 3G mobile phones, and increasingly other wireless communications technologies such as 802.11 wireless LAN (Local Area Network), coupled with palmtop PCs and PDAs, provide individuals with communications capabilities that would have been almost unimaginable a decade ago. The exchange of data files containing text, graphics, and embedded video/audio in real time, using mobile communications platforms, is now standard practice.

In recent years, research into wireless networking has been dominated by the perceived need for high bandwidth access to data intensive files with extensive graphical, video and audio content. Bluetooth has been heralded as the low-power wireless standard of the future, but it is very much a high-bandwidth technology, designed to integrate portable devices into this communications infrastructure, and is relatively power

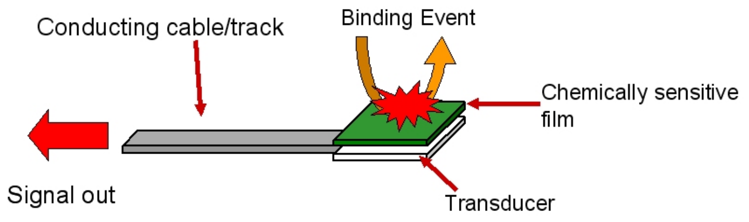


Figure 1. Stylised chemical sensor comprising a conducting cable or track to convey the electronic signal to the outside world, a transducer to sense the chemical signal and convert it into an electronic form, and a chemically sensitive film or membrane at which the molecular binding event occurs.

hungry. Similarly, wireless LAN (e.g. 802.11 standard) and particularly GSM mobile phones can provide personal gateways between portable computing and digital communications.

2. Chemical Sensing and Biosensing

Sensor research is driven by the need to generate a selective response to a particular analyte, for example, by a selective binding event such as occurs in host-guest complexation, enzyme-substrate reactions, antibody-antigen interactions, or other forms of biomolecular recognition. Hence many research papers are focused on developing a fuller understanding of the molecular basis for intra-molecular recognition, as this may ultimately lead to more selective devices that may find use in various futuristic applications. Coupled with this attention to selectivity is the need to provide a transduction mechanism, so that the binding event can be 'observed' from the outside via an electronic signal. Researchers typically will look to electrochemistry (e.g. potentiometry or voltammetry/amerometry) or spectroscopy (e.g. visible absorbance or fluorescence) for this signal. Often this is achieved via the presence of appropriate redox active sites or chromophores/fluorophores either as part of the molecular sensor itself, or as part of a sensing 'cocktail'. Success is dependent on the molecular binding event triggering transduction of the signalling moiety without adversely affecting the overall selectivity of the binding process.

Figure 1 shows the main features of a generic chemical sensor. The molecular binding event happens at a film or surface that contains sites designed to selectively interact with specific molecular targets. The binding event results in an electronic or optical signal that can be detected remotely and signalled to the outside world, and this signal conveys information about the molecular events occurring at this surface. Biosensors

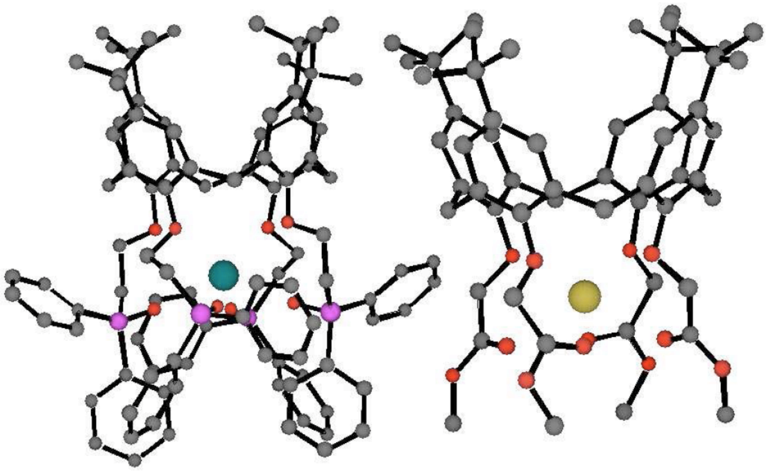


Figure 2. 3-d Energy minimised structures of t-butyl calix[4]arene molecular receptors with hydrogen atoms removed for clarity. Left is a sodium selective tetraester receptor and right is a calcium selective tetraphosphine oxide receptor. Carbon atoms grey, oxygen atoms red, phosphorus atoms pink. Sodium and calcium ions are shown in the energy minimised position within the negatively polar cavity in each case.

are similar, except that the binding events at the sensor-sample interface are generated by bio-receptors such as enzymes or antibodies in place of the chemo-receptors.

The 3-d structures of two ‘calixarene’ molecular receptors are illustrated in Figure 2. They contain certain structural features that make them very attractive for use in chemical sensors [2]. On the left is a so-called ‘tetraester’, which is highly selective for sodium ions, and on the right, a calcium selective ‘tetraphosphine oxide’. The ‘tetra’ part of the name tells us that there are four phenoxy repeat units in both cases that define the calixarene macrocyclic cavity. At the upper end of the structures there are t-butyl groups, and these, along with the phenyl groups render the receptors highly insoluble in water. The receptors differ in the binding groups substituted at the phenoxy oxygens at the bottom of the calixarene annulus, and these, together with the size of the cavity defined by the number of repeat units, to a large extent determine the selectivity of the ion binding behaviour of the resulting ligand. The tetraester (left) has four ester groups that define a relatively rigid cavity with the negatively polar oxygen atoms (and particularly the carbonyl oxygens) ideally suited for binding sodium ions. In contrast, substituting phosphine oxide binding groups results in a calcium selective receptor.

Sensors (ion-selective electrodes) incorporating these receptors are typically based on lipophilic membranes made from highly plasticized

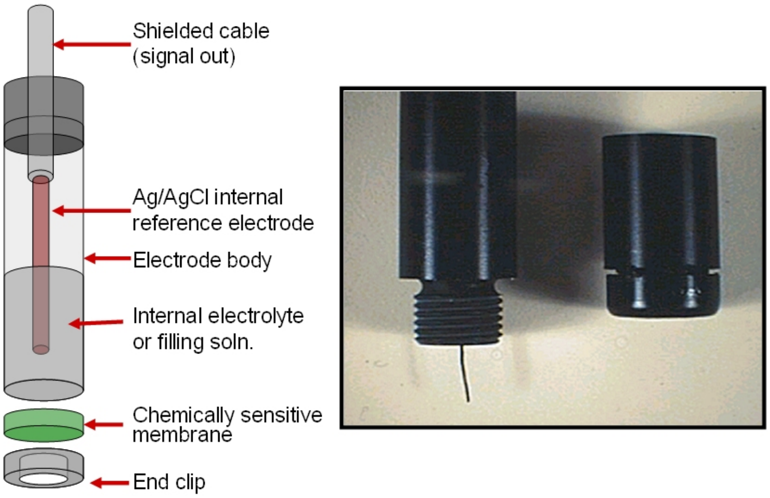


Figure 3. Components of an ion-selective electrode chemical sensor (left) and photographs of electrode body (right) showing electrode barrel with silver-silver chloride electrode, and screw-on electrode tip with end-clip for attaching the PVC membrane containing immobilised molecular receptors that will selectively bind specific target species.

PVC (60-70% plasticizer by weight), in which the receptors are effectively trapped in the membrane when exposed to aqueous samples. The mechanism of response is potentiometric; i.e. a galvanic cell potential is measured at zero current, and this is related to the ion-binding behaviour occurring at the membrane-sample interface. Selectivity is critical, as it is this that enables the user to relate the observed electrochemical signal to binding with the specific target ion. The sensors are made by attaching a membrane to the end of a hollow plastic tube which is filled with an internal reference electrolyte whose composition does not change, commonly a 0.1 M solution of the primary (target) ion chloride (see Figure 3). The membrane potential is sensed by a silver-silver chloride reference electrode (transducer) and the signal measured by a high impedance voltmeter. An external reference electrode completes the galvanic cell. The function of the reference electrode is to provide a stable, constant reference potential against which changes in the ion-selective electrode signal can be measured.

Until recently, it was accepted that the fundamental limit of detection of these sensors was at micromolar levels of the target ion in an aqueous sample, and the main application has been the determination of ions like sodium, potassium and calcium in blood samples, where the

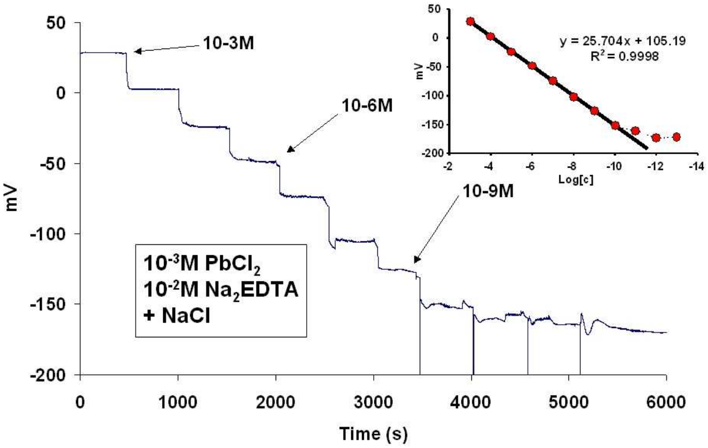


Figure 4. Response of an lead-selective electrode based on a calix[6]arene hexaphosphene oxide to sequential 10-fold dilutions of a sample solution demonstrating a very rapid Nernstian response down to sub-nanomolar concentrations of lead. The inset shows a linear Nernstian plot is obtained with almost theoretical slope (25.7 mV per decade) down to 10-10 M.

concentrations are relatively high. However, recent developments in the understanding of these sensors have led to breakthroughs in the operational characteristics, and sub-nanomolar measurements have been reported [3]. This has opened the door to many new potential applications for these low cost sensors, for example in environmental analysis, where metal ion concentrations are often sub-micromolar. Figure 4 shows results we have obtained with a t-butylcalix[6]arene hexaphosphine oxide based electrode in which the receptor is equivalent to the tetraphosphine oxide ligand illustrated in Figure 2, except that is has six repeat units that define a larger macrocyclic cavity, and results in a ligand highly selective for lead ions. Through careful optimisation of the inner filling solution (reference electrolyte) it is possible to inhibit transfer of primary ions from the typically highly concentrated inner solution to the outer membrane sample boundary region, and it is this process that masks the response of the sensor to sub-micromolar concentrations of the primary ion in aqueous samples. For example, in Figure 4 the response of a lead-selective electrode to sequential 10-fold dilutions of the primary ion is shown, and a Nernstian (theoretical) signal is obtained to sub-nanomolar lead ion concentrations (inset). In this case, the concentration of lead ions in the internal filling solution is reduced to 1.0 mM, and the free lead ion concentration further reduced using excess EDTA.

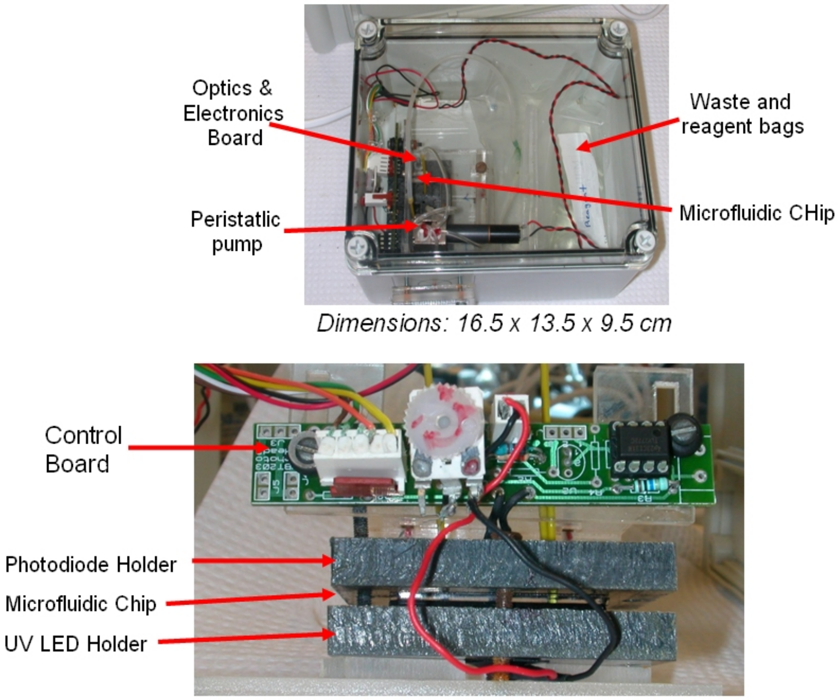


Figure 5. Photograph of an autonomous lab-on-a-chip system (top) configured for remote field monitoring of phosphorus in natural waters. Bottom is a closeup of the detector area of the system.

3. Miniaturised Analytical Instruments — Lab on a Chip Devices

In parallel with improvements in chemical sensor performance, analytical science has also seen tremendous advances in the development of compact, portable analytical instruments. For example, lab-on-a-chip (LOAC) devices enable complex bench processes (sampling, reagent addition, temperature control, analysis of reaction products) to be incorporated into a compact, device format that can provide reliable analytical information within a controlled internal environment. LOAC devices typically incorporate pumps, valves, micromachined flow manifolds, reagents, sampling system, electronics and data processing, and communications. Clearly, they are much more complex than the simple chemo-sensor described above. In fact, chemosensors can be incorporated into LOAC devices as a selective sensor, which enables the sensor to be contained within the protective internal environment. Figure 5

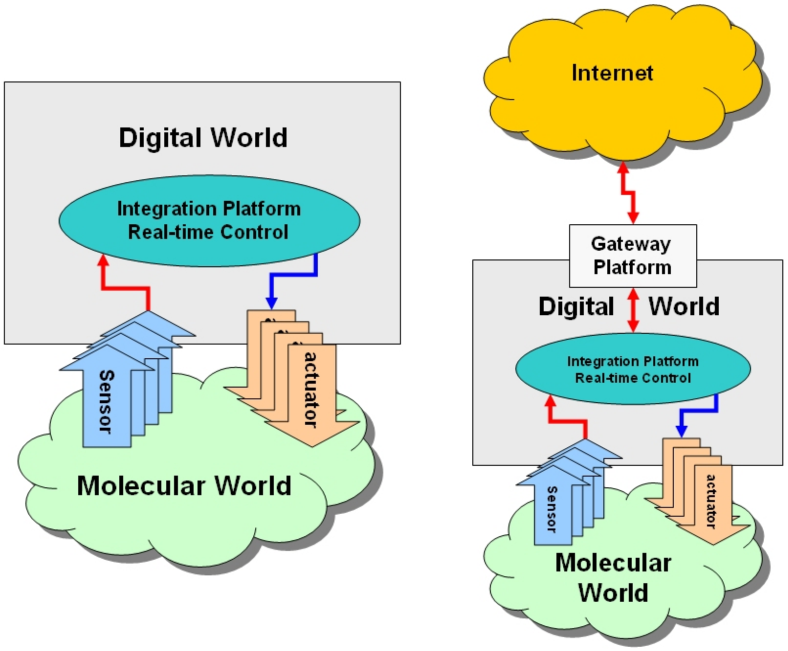


Figure 6. Left: Conventional control loops provide a localised interface between the real and the digital world. Sensors targeted at important control parameters feed information into digital control routines that can respond via actuators e.g. to maintain parameters within specified limits. Right: A vital step on the route to the realisation of the concept of internet scale sensing is to adopt the principle that all analytical measurements should be capable of being internet-linked. The localised control of important parameters is maintained, but the information is shared via the internet with external users [4]. (Reprinted with permission from Anal. Chem., August 1, 2004, 75 (15), 278A-286A. Copyright 2004 American Chemical Society.)

shows a relatively simple analytical device configured for performing autonomous optical (colorimetric) reagent based measurements. In this case, the sample is accessed via a microdialysis membrane and is drawn into a microfluidic manifold where it mixes with a reagent cocktail that generates a colour if a specific target species is present in the sample. The colour of the sample is measured with a photodiode using a light-emitting diode (LED) that has an emission maximum coinciding with the absorbance spectrum of the generated colour. The analytical literature is awash with papers on chemical sensors, biosensors and microfluidic (LOAC) instruments. However, for reasons that will be outlined below, these devices, unlike physical transducers, have not really been combined into extensive 'sensor networks'.

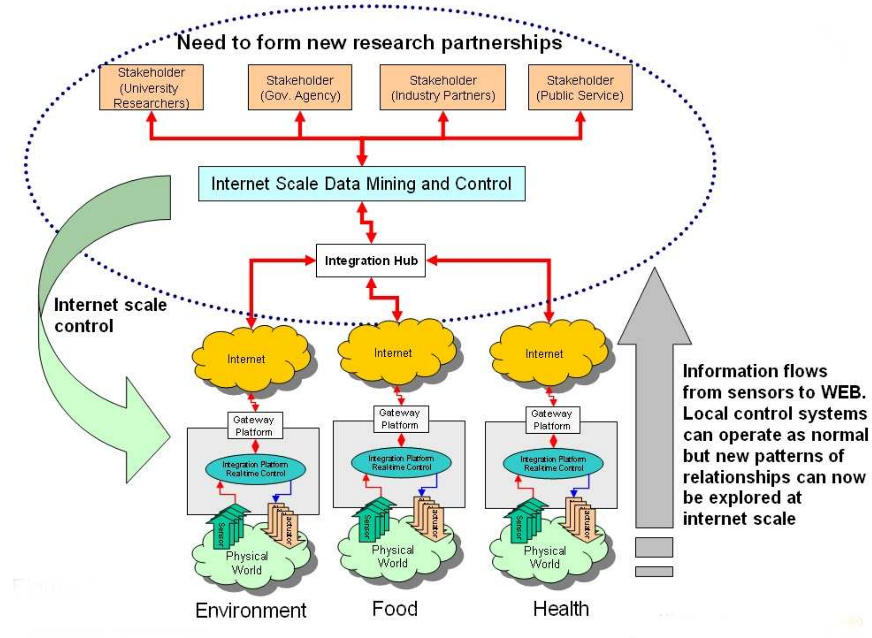


Figure 7. Widespread implementation of internet-enabled analytical measurements leads to Internet Scale Sensing, a new and powerful vision that links various application sectors (environment, security, health) and a wide variety of users [4]. (Reprinted with permission from Anal. Chem., August 1, 2004, 75 (15), 278A-286A. Copyright 2004 American Chemical Society.)

Internet Scale Sensing and Control

Internet scale sensing [4] conceptually involves large scale deployment of large numbers of sensors or sensing devices into wide area networks, sometimes referred to as sensor nets or sensor meshes. Figure 6 illustrates the basic principle. A conventional control loop consisting of one or more sensors and actuators (left) becomes part of a global information exchange through implementation of the basic principle of internet enabling every analytical measurement. This immediately enables external browsing of sensor status, external programming of control parameters, and feedback of information to individuals and to other devices. Widespread adoption of this principle leads to the emergence of 'internet-scale sensing and control systems', in which millions of sensing devices and actuators are linked in a seamless manner with a wide variety of users, ranging from individuals, to Government agencies, industrial users or public service providers, across many application sectors (Figure 7). However, the real value lies in the realisation that large-scale sensor networks provide much more information than is predictable from simple linkages between localised collections of individual sensors. In fact, there is tremendous potential for the discovery and use of entirely new types of relationships between information extracted from this data 'continuum', which will give rise to new business opportunities, and the emergence of completely new markets. This has been identified by Ron Ambrosio and Alex Morrow, from IBM's Watson Research Centre, as one of the key developments that will fuel rapid developments in the Information and Communications Technology (ICT) sector in the coming years [5]. Other major players are moving into this research space. Intel has established the Intel-Berkeley Research Lab to develop sensor 'mote' technology — motes are low power communications platforms with integrated sensors (temperature, light etc.), and built-in capabilities for adding other sensors.

Finding field demonstrators that are scientifically interesting, field deployable and available at a cost appropriate for the envisaged scale is a challenge. The Berkeley team has assembled a 50-node sensor network to monitor seismic activity across the campus, and a 32 node sensor network linked by satellite communications via a basestation has been used to study the microclimates associated with the nesting sites of storm petrels on Great Duck Island, Maine. Each node included a habitat monitoring kit that could monitor light levels, heat, temperature, barometric pressure and humidity [6, 7].

At UCLA, Deborah Estrin is heading up the 'Centre for Embedded Networked Sensors' or CENs, a $40 million, 10-year NSF-backed centre

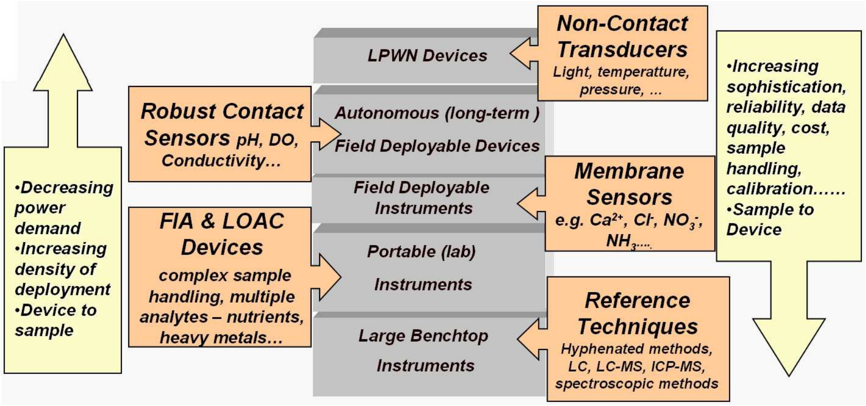


Figure 8. Analytical instruments can be arranged into an hierarchy in terms of highly correlated factors such as sophistication, capabilities, operational costs, and degree of autonomy. There will be a significant correlation between these factors and density of distribution throughout the networked world. Providing effective communications between these layers provides routes to validating data from low cost devices using more reliable data obtained from sophisticated devices [4]. (Reprinted with permission from Anal. Chem., August 1, 2004, 75 (15), 278A-286A. Copyright 2004 American Chemical Society.)

[8]. Parallel to this, the European Union has invested EUR 111 million in wireless research under the 6th Framework programme [9], and the indications are that this will be significantly increased in the forthcoming 7th Framework programme. The scale and extent of investment and research activity is a clear signal that this area is now receiving priority attention from academic researchers, research agencies and industry.

4. Analytical Device Hierarchy

Like the digital communications industry, analytical devices can be layered into an hierarchy in terms of their complexity, degree of autonomy and need for external services (Figure 8). Lab based instruments are already heavily integrated into conventional digital networks, usually as part of a site-based network. In principle, this information is readily available, but in practice, it tends to be restricted to the site, as it typically needs sophisticated work up and interpretation. Likewise, field based instruments, and particularly devices employed in an autonomous manner, have an immediate demand for integration into digital networks, but as these are placed increasingly at more remote and less serviced situations, conventional networking strategies become less feasible. As this trend ramps up, and the numbers of devices operated in an autonomous manner increases, the need for low power operation becomes rate determining. Clearly, the least sophisticated of these devices will be distributed in the largest numbers, and will essentially operate on almost zero bandwidth (e.g. they may send only a few bits information to indicate a threshold has been crossed). Low bandwidth is of course very unattractive to the communications industry, as their business model tends to be based on the volume of data transferred (hence the attractiveness of large audio and video files). In contrast to data quantity, the attractiveness of wireless sensor networks lies in the importance and value of the information they can provide.

At present, research into the most densely distributed layer (very low cost, autonomous devices) is dominated by the use of physical transducers such as pressure and temperature sensors that do not have to make an intimate contact with the sample/environment (i.e. they can be totally encased within a protective cladding and still function). Introduction of chemical sensing capabilities is happening through the use of 'old-reliables' such as pH and dissolved oxygen (DO) sensors, as these are known to be fairly robust. Sensors that depend on polymer membranes or surface films for response generation will be affected by exposure to the sample over time, so more sophisticated devices that incorporate calibration routines are typical, which drives up the cost base, making dense distribution economically unviable. This is the paradox at the heart of the chemical sensor/biosensor failure to demonstrate large scale sensor networks — we need reactive surfaces to generate the analytical signal and provide the molecular information, but we also want these surfaces to remain unchanged over long periods of exposure to the real world, in order to enable simple, low cost, calibration free measurements to be made.

Lab-on-a-chip (LOAC) approaches in which the analytical measurement is performed within a sheltered microfluidic environment is an attractive option, but these are also too costly to deploy in large numbers at present (see discussion below). The challenge for analytical scientists is to move devices towards the more densely distributed layers by driving down the cost base while simultaneously maintaining reliability and quality of the analytical data. Clearly, there will be increasing use of physical transducers and reliable chemical sensors in networked systems. Relatively simple measurements such as turbidity, colour, pH and conductivity can provide important general information about water quality throughout a complex distribution network, enabling contamination to be detected at an early stage, and corrective action to be taken before contaminants spread throughout the entire system. The success of these

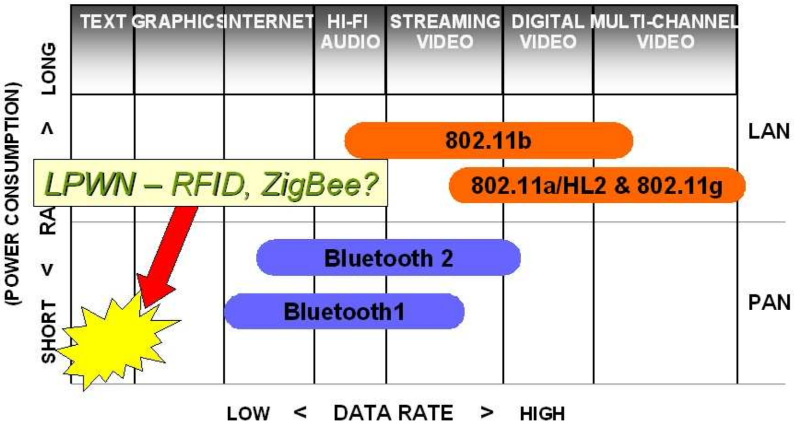


Figure 9. A variety of wireless options are becoming available. The 802.11 technologies are high bandwidth and relatively high power consumption, and are best suited for serviced areas. It is the basis of the emerging 'hotspot' services provided at hotels and airports. While Bluetooth has a lower power demand, in its current form, it is more targeted at 'Personal Area Networks' or PANs of peripherals. ZigBee appears to be the most attractive option for low power wireless sensor networks although the short distance between nodes is a serious limitation for field deployed devices. The ideal specification (starred area) would extend the distance of the ZigBee protocol while keeping the power consumption as low as possible [4]. (Reprinted with permission from Anal. Chem., August 1, 2004, 75 (15), 278A-286A. Copyright 2004 American Chemical Society.)

sensors will in turn drive demand for more complex measurements to be integrated into distributed sensor networks.

5. Networking Options

Network technologies have already made a major impact on analytical science. It is now standard practice to network analytical laboratories, and specialist services such as Laboratory Information Management Systems have been developed specifically to integrate laboratory information with conventional administrative networks in large organisations. Every instrument, down to the humble pH meter has a PC interface, and can be easily networked. The explosion in demand for mobile access to communications, has driven the rapid development of wireless networks such as the 'wireless hot spots' based on IEEE 802.11 standards that are appearing at airports, hotels, cafes and universities. These offer high bandwidth access, typically to users with laptops and palmtops seeking email or WEB access, but could provide an infrastructure for networking analytical devices. Bluetooth is another wireless network technology targeted mainly at wireless connectivity between peripherals such as mice, keyboards, headsets, printers, devices like mobile phones, palmtops and PDAs, and home appliances in a ‘personal area network’ or PAN [10]. However, both 802.11 and Bluetooth are designed for conventional network communications, as is evidenced by the high-bandwidth specification, and relatively high power consumption (Figure 9). Therefore, while these technologies will undoubtedly make it much easier to connect analytical devices within a building, they are unlikely in their present forms to be suitable for long-term autonomous operation in remote locations.

In contrast, the ZigBee Alliance, involving companies such as Honeywell, Mitsubishi Electric, Phillips and Motorola, is developing hardware and software communications standards focused on low bandwidth, low-power consumption applications [11], which is potentially more interesting for autonomous analytical devices, although the limitation at present is in terms of distance (less than 100 metres between nodes), and typically just a few metres (ZigBee is being promoted mainly for linking items within the home). The future is likely to comprise a number of interlinking technologies, like ZigBee, bluetooth, 802.11, mobile phone technologies such as GSM/GPRS/3G (Global System for Mobile telecommunications/General Packet Radio Service/third generation) and conventional cabled networks. These technologies will gradually integrate and appear seamless to the user, and analytical devices will make use of them all, with density of deployment correlating with low cost, low power consumption technologies, where the limitations will be low bandwidth and short distances between nodes.

6. Integrating Chemical Sensors and Biosensors with Wireless Networks

Clearly, there is considerable research activity targeted at incorporating sensors into low power wireless networks (LPWNs). However, the sensors employed in these studies are almost entirely transducers measuring physical parameters such as heat, light, humidity, pressure, position etc. While the information available from these sensors is very valuable, and important advances are being made through their use, they cannot fulfil the vision of bridging the digital and molecular worlds. This next step will require the introduction of chemical sensors and biosensors into LPWNs.

However, realisation of the LPWN-compatible chemical sensors/biosensors critical to the realisation of a pervasive sensing vision depends on the development of devices that are capable of massive scale up on the one hand (and are therefore very low cost, suitable for mass production) and very reliable (capable of autonomous operation for at least one year is a typical target for environmental applications, five years for biomedical implants).

The key challenge therefore is to identify stable analytical chemistries and methods that can be incorporated into these devices, as this will be the basis for the underlying quality of the multitude of analytical signals that will be fed into the web-based networks for higher-level decision making. Therefore, the delivery of the overall vision depends on the ruggedness and reliability of the analytical devices, and the knowledge held within the analytical community becomes the key to unlocking the next revolution in communications.

7. Scale-up Issues for Densely Distributed Analytical Devices

Cost

The successful integration of chemical sensing and biosensing into the broader vision of the 'context-aware world' depends on the availability of widely distributed (pervasive) networked sensors that feed reliable data into the information layer. Electronics and communications substructures (nodes) are still too expensive (80−150). Motorola [12] is incorporating ZigBee wireless protocols into all their pressure and acceleration sensor chips, to facilitate the development of sensor networks for distributed monitoring, control, and automation, but the chips for more generalised use (i.e. with other sensors) are not commercially available. The Berekely Mote technology is now available commercially from Crossbow Technologies Inc., in a number of developer kit formats that typically include motes, sensor boards, and relatively simple user interface software that runs under TinyOS [13], [14]. The motes incorporate ad-hoc networking capabilities and enable demonstrator applications to be developed relatively easily. The latest manifestation is a mote platform around the size of a 1 euro coin (see Figure 10) that can transmit signals approximately 100 m.

Obviously, scale up and cost are reciprocally related, and while relatively small-scale deployment for research purposes is possible at current costs (dozens of devices), unit costs must be driven down by orders of magnitude before large scale deployment of devices is feasible. However, the vision from the engineering community is that 'everything that costs over $25 except food will be connected to the Internet' [15]. To quote Kris Pister, from UC Berkeley, 'by 2010, RF circuits capable of trans-

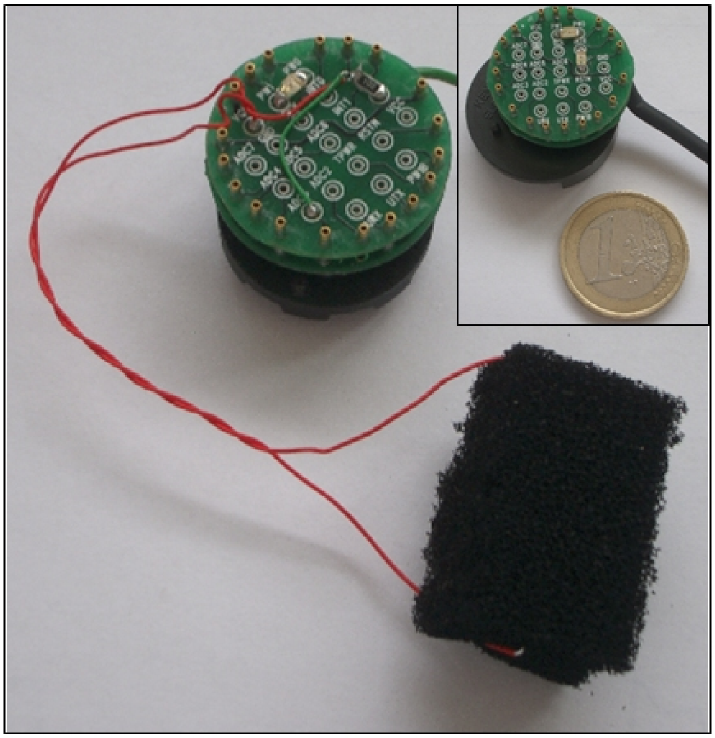


Figure 10. Wireless Mote platform available from Crossbow Technology Inc. The photo shows the platform attached to a small portion of smart foam we have developed for sensing compression e.g. in smart fabrics for monitoring breathing.

mitting 100 m at low bandwidth (up to 100 Kb/s) will cost $0.10, and consume very little power (10nJ/bit). The devices will have the capability of running for perhaps 10 years from a standard battery source' [16]. The implication is that it will cost virtually nothing to include wireless communications capability, and therefore it will become ubiquitous, and will be an almost universal standard feature.

Reliability

In order to realise their potential within this vision, a critical requirement for chemical sensors and biosensors will be stability over long-term deployment. For analytical measurements, the key component is the sensing membrane or film which, when exposed to the sample, generates a sensitive, selective signal that links a molecular binding event to the value of a digital number. Hence the ultimate functionality of a chemo/biosensor network depends on the nature of these molecular interactions. If these are subject to interference by non-specific binding, or changing characteristics due to instability over time, then a practical system cannot be realised, as it will impossible to distinguish real from spurious events, leading to unacceptable levels of false positives and negatives. A major challenge therefore, is for analytical scientists to demonstrate long-term stability of reagents, molecular receptors, films and membrane cocktails such that the chemistry/biology of the analytical measurement is not the limiting factor in terms of overall reliability.

The analyst's traditional strategy for coping with stability is to calibrate regularly. But calibration of autonomous devices involves additional complexity in terms of flow manifolds, valves and pumps, stable standards, and waste storage. Hence remote calibration and massive scale up are incompatible strategies in the medium term, although autonomous lab-on-a-chip devices with built-in calibration could be deployed on a moderate scale, perhaps as more sophisticated nodes against which simpler, more densely distributed but dumber devices targeted at the same analyte could be remotely calibrated. A starting goal is to find reagents that will be stable for up to one year, as this will help simplify the calibration issues.

We have looked in detail at the analysis of nutrients in natural water, as this is of considerable interest globally, in terms of the overall effect on water quality, and in particular, the prevention of algal blooms which have become an all-too familiar problem in many countries. Bearing in mind the need for inexpensive components and the requirement of low-power operation, we have focused on colorimetric detection using LED/photodiode detection in a microfluidic manifold as a generic approach. So far two reagent methods have been identified as meeting the 12 month stability requirement (calibration slope should be better than 90% of the original slope after 12 months); the yellow method for orthophosphate [17], and the molybdenum blue or Bertholet method for ammonia [18]. Interestingly, the yellow method was found to be preferable to the more common indophenol method as the latter requires the use of ascorbic acid in the final reduction stage, which drastically limits the overall stability of the reagent cocktail. Note that the yellow method only became a viable option very recently with the commercial availability of UV-LEDs, as the absorbance maximum (380 nm) of the phosphate complex is too low for detection with pre-existing LEDs [19].

For ammonia, the commonly employed molybdenum blue method was examined. In this case, there were a number of issues. For example, the standard method requires the use of phenol and hypochlorite. Phenol is unsuitable for health, safety and environmental reasons, and hypochlorite is commonly regarded as unstable. We found that salicylate could be substituted for phenol, with little affect on sensitivity and a relatively small movement of the absorbance maximum, and hypochlorite is stable if stored carefully, and there is very low contamination by certain catalytic metals that accelerate decomposition, such as copper and iron [20].

An issue with reagent based methods is the amount of reagent consumed annually. For example, if 1 litre of reagent is consumed per year, then scale up to millions of devices is not feasible, from the point of view of re-supplying reagents, and of disposal of waste reagent generated. Scale up in numbers means equivalent (or better) scale down in reagent use. This is possible using LOAC devices. For example, at a flow rate of 1 uL/minute, 6 minute sample turnaround time, and a requirement of 1 analysis per hour, less than 50 mL of reagent is required for 1 year continuous operation. While this is still too much for massive scale up, it does fit into the scenario that LOAC instruments could be less densely distributed at more sophisticated nodes within the network.

Alternative strategies are to use arrays of single-shot sensors (ideally reagentless) manufactured to a very high level of reproducibility, and packaged to ensure the device surface is protected from change during storage. While this can reduce significantly the need for calibration, and provide reliable data for extended periods of time, it is not possible at present to produce the required instrumentation at a low enough price to make very large scale up economically viable.

Sampling

For LOAC devices, the use of dialysis sampling in aqueous environments is an attractive option for a number of reasons:

1. The dialysis membrane protects the microfluidic manifold from ingress of particulate matter that can block the narrow channels or damage valves/pumps.
2. A stopped flow approach can be employed using dialysis sampling which allows effective transport of low molecular weight components from the sample across the dialysis membrane and hence the dialysate will accurately reflect the composition of the sample.
3. The membrane produces a semi-sealed unit that enables waste reagents to be contained after use (waste bag fills as sample bag empties).

However, current forms of LOAC devices have many components external to the microfluidic chip such as valves, pumps, power supplies, electronic circuitry, and reagent/waste storage units. While these devices are a major advance on pre-existing autonomous instruments and could be deployed on a reasonable scale, they are typically too large, consume too much power and are too expensive for high-density deployment.

Nevertheless, LOAC devices hold considerable promise for short to medium term solutions to analytical applications that require medium or low density deployment, particularly for environmental and security monitoring of chemo/bio targets detectable via well-known reagent based analytical methods that can be transferred to a microfluidic platform. Perhaps the greatest barrier to more widespread deployment is the current use of scaled down conventional pumps and valves for controlling liquid movement throughout the manifold. Not only do these devices contribute greatly to the overall cost and size of the device, they are also prone to malfunction, and are usually the greatest source of power drain by the system. Research into novel methods for controlling liquid movement in microfluidic channels is therefore particularly important. One approach that appears to hold considerable promise is the integration of materials that will swell or contract under external photonic or electronic stimuli. A recent review summarises the many materials that are currently under investigation for this purpose [21]. Successful integration of such ‘soft’ valves and pumps would therefore be a significant advance for these devices, as they are inherently low power, low cost, much more tolerant of microparticulants, and would produce more compact microfluidic platforms.

8. Chemo- & Bio-warfare Agents

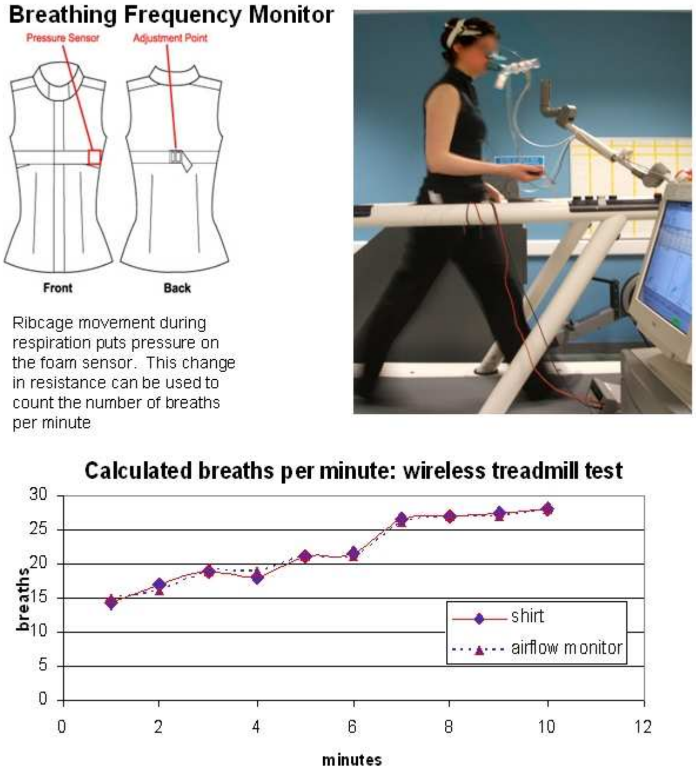
Sensor networks capable of providing advanced warning of the release of a biowarfare agent, and tracking its geographical spread is a very attractive vision. However, there are many issues and barriers inhibiting the successful widespread deployment of such devices. For example, in the case of anthrax, the requirement to detect down to single bacterium in 100,000 litres of air requires a sophisticated sampling and sample processing regime. To meet this type of need, it is critical that the presence of the target is detected when present at a very low threshold, with no false negatives or positives [22]. Such requirements pose significant challenges for the analytical community. The development of reliable, low-power, distributed networks of instruments capable of detecting trace levels of such targets is beyond the current state-of-the-art, and a sustained investment of R&D resources will be required over a considerable period of time to develop breakthrough technologies. In addition, the reporting of an event (e.g. release of a biowarfare agent in a public place) is a complex issue, as has been highlighted in a recent revue of the issues [23]. For example, there are temporal dynamics that underlie the layered information feedback loops to various user groups. Clearly, the information relayed to the public at rush hour in a busy city must be carefully managed to avoid triggering mass panic. The information management system must therefore recognise the potential effect of feedback on to various stakeholder groups, and how this effect varies with respect to time, and location. However, progress is happening, as demonstrated by the recent report of an autonomous pathogen detection instrument for the detection of aerosolized bacillus anthracis and yersinia pestis [24]. Such devices necessarily integrate multiple operations normally carried out in specialised laboratories such as sample processing, separation, amplification and orthogonal detection methods to ensure the analytical result is correct, and this leads to a device that is large and heavily serviced in terms of power requirements and reagents, and therefore unsuitable for large scale deployment in its current form.

Undoubtedly, further integration of analytical processes (and particularly sample handling) will happen, which will make denser deployment possible. The widespread availability of effective and widely distributed monitoring of chemo- and bio-warfare agents will reduce the incidence of false alarms and copy-cat events, and may reduce the effectiveness of these weapons, which often rely on the fear of what might be present, rather than the reality.

One idea recently reported in the media is to integrate sensors for specific threats into mobile phones [25]. These would essentially be passive until the sensor signal crosses a critical threshold, at which point a set message is sent to a pre-determined location. Coupled with GPS information inherent with every phone, this provides a very simple route to early detection of the source of the release of a potentially lethal agent, with signals from other phones providing cross-validation, reducing the potential for false negatives and false positives. Furthermore, as mentioned above, this would enable the dynamics of the event to be monitored, as a plume spreads through an area, while simultaneously providing a means to send information to individuals and emergency services. However, given the current status of biosensor development, it is unlikely that sensors with the required specifications will be available for some time. A more likely scenario for passive background monitoring of threats would be to incorporate threat detectors into vehicles as a standard component. This would enable more complex services and diagnostics to be provided and therefore reduce the operating constraints, making device deployment much more likely than in mobile phones. Vehicles are rapidly becoming integrated into communications networks through GPS-based route planners and GSM phone capabilities, and have sophisticated internal sensing and communications systems already in place. Threat detection could therefore be seen as a logical extension of these capabilities, which takes advantage of the pre-existing infrastructure.

9. Sensor communities and group behaviour

Moving from localised, lab based analytical methods to widely distributed sensor networks requires new strategies to deal with issues such as calibration, data validation and device diagnostics. In terms of the device hierarchy described above, the main challenge lies with the most densely distributed and least sophisticated devices, as incorporation of calibration, validation and diagnostic procedures requires a more sophisticated instrument and therefore less dense distribution. This is a critical issue, as scaling up to the use of large numbers of dumb devices inevitably will give rise to increasing instances of false positives/negatives and device malfunctions that must be identified and discarded from the overall data population. On the other hand, the use of sensor communities rather than single devices allows group behaviour strategies (e.g. collaborative reasoning) to be employed to help identify spurious signals and device malfunction. For example, in a densely distributed sensor network monitoring air or water quality, it is very unlikely that a real event will occur on a single device only. For real events, threshold crossing will normally occur in a number of devices clustered in a particular location,



Ribcage movement during respiration puts pressure on the foam sensor. This change in resistance can be used to count the number of breaths per minute

Figure 11. Comparison of a wearable foam sensor integrated into a shirt, and a reference airflow monitor (facemask) for monitoring breathing during treadmill experiments. The results (bottom) indicate that these types of innocuous wearable sensors can provide important information on general heath indicators such as breathing [27].

and the dynamics of the event can be followed by the temporal development of the signal pattern obtained from these simple devices. An additional level of functionality can be offered by using autonomous mobile (robotic) devices that move towards an event signalled by a device in order to locate the source, and to validate the event. Such swarming-like behaviour can be followed using GPS data, and the position and relative abundance of the devices around a particular location can in itself provide diagnostic information about the location and dynamics of an event.

10. pHealth

Personal Health or pHealth is an area of great potential for a number of reasons. Unlike remote environmental monitoring, the wireless communications network is already in place, and individuals have their own personal gateway through the mobile phone. This means that the existing infrastructure can be used to provide pHealth support, and applications will be rolled out over the next few years. Examples already emerging include smart fabrics for monitoring personal heath indicators such as breathing, heartbeat, and movement (changes in gait or emergence of tremors) in which the sensing component is formed from a functionalised fabric, rather than a discrete sensor attached to the person [26, 27]. Materials like lycra and foam can be converted into stretch and compression sensing components and integrated into clothing (see Figure 11). This will be part of a more extensive move to develop pHealth products. Examples will range from electronic personal medical records, to fully integrated diagnostics and 'wellness' systems for elderly people (i.e. detecting movement, location, application of therapeutic agents, electronic monitoring of diagnostic data etc.). One of the main players in this area is Intel. Despite being an application agnostic company, Intel is not waiting for the potentially lucrative health related markets of widely distributed sensing to emerge spontaneously [28]. Rather, it is actively cooperating in pilot projects to demonstrate the tremendous benefits of this technology from the ground up, knowing that this will in turn drive growth in future markets.

11. Conclusions

The incorporation of analytical devices ranging from tiny sensors, to hand-held instruments, and autonomous field devices will happen during this decade. It is important for scientists to appreciate the implications of this process now, as it has the potential to generate truly disruptive technologies that will have a profound effect on the way people live. In medicine, it has the potential to enable people to remotely monitor disease markers and apply therapies, while still being in intimate contact with specialists who can access their data instantly via the web. In agriculture and food, it will facilitate quality tracking through the distribution chain, 'from harvest to home', and in the environment, it will allow access to data gathered from multiple locations by a variety of users, including local communities and individuals, as well as specialists. In fact, environmental sensing is already well advanced at this time, as distributed geo-sensing has been an area of very active research for many years, for example through satellite-based spectral mapping. Complementary to this information is that available from widely distributed surface-based sensors. Hence this community is one of the first to realise the potential of networked sensors. The first workshop on Geo-sensor Networks was recently held in Portland, Maine and the report on the meeting touches on many of the issues highlighted in this article including programming sensor networks, device scalability, mobility of sensor nodes, and higher-level modelling and reasoning from large data sets [29]. Understandably, another area of intense research focus is security and threat detection, particularly for applications such as the early detection of air/water borne bioactive/chemoactive/radioactive warfare agents, and the associated approaches for alerting of agencies, emergency services, and the general public should this occur; i.e., personalisation of feedback information. In fact, the merging of data from this continuum of sources and its accessibility via the web will open up entirely new areas of research, such as linking of incidences of illness to environmental or food quality parameters, or correlating the effectiveness of community based health management with the individual's behaviour (was the marker measured and the drug taken at the correct intervals, was the correct dose taken?).

It is also clear that as this vision is gradually realised, there will be very significant ethical and moral issues related to the type of information stored, how long it is stored for, who gets access to it, and the conditions under which various users can access the data. As with any technology that generates information of direct impact to people and societies, there is the potential for beneficial use, and for abuse. Given the tremendous power of sensor networks to deliver highly personalised information, it will be vital that issues related to data security on the one hand, and the definition of an ethical framework for proper use on the other, are also addressed. Delivering the vision will clearly require new alliances of industries, Government agencies, public service providers, university research centres, and community groups. The scale of the opportunity is truly enormous, as is that of the research effort required to deliver it.

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